Secretary of Agriculture
Mr. Dan Glickman
Dept. of Agriculture
Agriculture Building
Washington, D.C.

Aug. 20,99

Dear Mr. Secretary:

Fraudulent Biotech Health Reviews

As a former vice-president of the largest genetics research firm in the U.S.A. and as a person with more than 50 patents on toxic materials as well as having developed the first triazole systemic fungicide for wheat, I believe it is my place and right to inform you of fraud in the approval of the biotechnical product rBGH(recombinant bovine somatotropin).

Our laboratory was selected by the Senate of Canada, Committee on Agriculture and Forestry, to testify on the data concerning this matter. In that testimony, April 26th ,1999, we suggested that the approval process for rBGH was fraudulent.

Below, we will explain why in succinct terms.

1. The statistically significant effect of the milk from rBST/rBGH treated cows on liver growth was omitted in all pre-approval reviews of rBGH. These effects are found in J. Nutrition 120:514. 1990, by Groenewegen et al. They were simply avoided in all discussion. And, this report constitutes the only whole milk health study as a food for human prior to its approval.

2. The entire field of diabetes promotion by milk antibodies was omitted as was the entire area of diabetogenic materials which might arise in rBGH milk. The report, Journal of Metabolism (page attached) by Sonnenberg, was omitted. This 1965 report on bovine growth hormone concerned tryptic digests tried on humans, it concluded that bovine growth hormone enhanced diabetes in diabetics. (Medical costs in the USA are 15-20% related to treatment of diabetes)

3. Rather than answer directly and promptly, questions from Congressman Klug representing a large constituency here, the FDA personnel involved told the Congressman they would see what the W.H.O. expert committee said. They didn't tell the public and Representative Klug that they were an integral part of the Committee. They then proceeded to cover-up the negative effects in the only health test ever done on rBGH milk(the 14 days oral study by Groenewegen in which liver effects were noted) and put off replying to Rep. Klug for many months. They did this by omitting the data in their W.H.O. review. Their reply to Rep. Klug lacked any data what so ever. Representative Klug had to demand a visit to F.D.A. to determine why there was no replies to his letters..

4. As it stands today there is a complete lack of chronic health data on rBGH as well as rBGH milk except for the recent publication connected with the Canadian review which showed

Fairview Industries, Inc., 2836 Jefferson Dr. , Blue Mounds, WI. 53517

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antibodies were formed in rat when orally treated with rBGH. The chronic effect of having an antibody to a recombinant growth hormone circulating for a life time of exposure in children or adult would naturally not be known.

5. The Deputy Director of the FDA was employed by Dr. D. Kessler. He is Dr. Steven Sundlov. He is a former associate of Dr. Robert Collier, Monsanto's Director of Animal Health Research, when they were professors at Un. Of Florida. The public must ask now, how did a former associate of Monsanto's vice-president come suddenly to FDA after appearing as an independent reviewer of rBGH on a Food Advisory Panel in 1993. Was he actually reviewing his FDA job while supposedly an independent reviewer on a panel discussing safety?

Dr. Sundlov stated on national TV(CBS Morning, 1/24/96) that rBGH had been tested as much as a human drug, "tested for years". This is false. This is a lie. Human drugs require exhaustive metabolism and chronic health data. rBGH was evaluated 90 days on rat in any standard health study. The chronic health tests were completely omitted, such as those tests used to quantify and qualify a pesticide residue or food suspected of being a chronic poison.. And, on July 2nd, by interview in Representative Klug's office , we learned that no metabolism data were done on the synthetic hormone. The only substance measured in the milk was parent hormone, no metabolites were examined. Therefore, in this regard no statement can be made as to what the content of the milk is as regards rBGH metabolites and their biological activity. The initial study of bovine growth hormone resulting in the diabetes statements was done using digested preps of bovine hormone. Such materials may be more readily absorbed than rBGH as a zinc complex. Further, some research is Japan has shown that whole lacto-albumin is absorbed in human and reaches human breast milk.

The promotion of diabetes by serum proteins in human as related to milk as well as human auto-antigenic materials suggests that we must exert extreme caution. In one report from Cyanamid there showed a significant leakage of cow serum into the milk of cows on rBGH. Thus, it is reasonable to expect that the biology and ecology of human diabetes will be effected by rBGH milk. It is more reasonable to assume injury is likely than to assume safety without any, not a shred, of chronic health data and with so many reports showing some type of oral effect.

Avoiding the discussion of previously published negative health effects such as arose in the Groenewegn report as well as the attached report by Sonnenberg constitutes fraud. If a chemical firm were not to relate some serious health effect to E.P.A. which had occurred in their manufacture or research on a commercial material, it would be in violation of the law.

As concerns the co-produced hormone insulin-like-growth factor-I, as a society we should not be tampering with this material in foods. In a recent W.H.O report on rBGH milk they dismiss this material's various forms(binding to other materials) as if it were trivial. Mr. Secretary, this hormone need not be taken up by the human to exert its effects. All it needs to do is contact the surface of a colon or gut lining cell to enhance cell division . Its concentration has been discussed with minimal availability and chronic health studies. For example, no gel electrophoresis studies of rBGH milk were done at all looking at the new materials which might arise from the stressed cow. (Said cows have depleted bone marrow function after three weeks of

usage, see Monsanto F.O.I. document)

We are glad the Canadian government has held hearings on rBGH data and stopped this utter nonsense of placing materials and modified foods in the diet without any chronic health data. The action is long overdue. Action should be tkaen by the U.S.D.A. immediately to stop sale of rBGH based on the enclosed data on diabetes and complete lack of chronic health data on rBGH milk or rBGH metabolites.

The lack of chronic health testing of novel proteins in recombinant genetic foods has already become a risky and unwritten policy.

Concerning document 2 attached the American and Canadian public are entitled in my view to a complete study of the components of the serum contents changed by the use of rBGH as shown in Dairy Science vol. 72, no. 6, 1989, as related to diabetes risk. Some serum components have already been identified as human autoantigens in diabetes and in Finnish studies of diabetes effects in children. Thus, there is no excuse what-so-ever for not recognizing and syudying this matter.

Sincerely,

William von Meyer

Dr. William von Meyer,Ph.D

Table 5.—*Source, Degree of Proteolysis, and Biological Activity of Growth Hormone Preparations*

Growth Hormone Preparation		Lot No.	Min. of Digest.	Moles KOH/Mole Protein§	Growth Hormone Potency USP Units/mg.
BGH	A° and D	Average of 19 lots	0		2.03
BGH-digest	D	F-1-260	5	2.7	1.32 ± 0.65
BGH-digest	D	F-1-245-1	10	5.3	1.39 ± 0.37
BGH-digest	D	F-1-262	10	6.3	0.58 ± 0.21
BGH-digest	A	F-11-157	18	6.9	0.72 ± 0.24
BGH-digest	A	F-11-105	30	9.1	0.37 ± 0.10
BGH-digest	D	F-1-245-11	30	9.8	0.38 ± 0.11
BGH-digest	A	F-11-80	60	13.8	0.08 ± 0.03
BGH-digest†	D	F-1-200-1	60		0.23 ± 0.05
BGH-digest†	A	F-1-181-1	120		0.25 ± 0.05
BGH-digest†‡	D	JD-160	60		0.62 ± 0.15

°A or D, respectively, indicate BGH prepared from Antuitrin G or by method of Dellacha and Sonenberg.[5]

†Digestion performed in borate buffer.

‡Prepared from partially purified growth hormone.

§Assumed molecular weight of 45,700.

of proteolysis indicated by base uptake, the electrophoretic patterns, and decreases in biological activity in rats appeared consistent.

Effects in Diabetic Patients. There was significant aggravation of diabetes associated with the administration of 3 tryptic digests of BGH, i.e., 10 min. (study 2), 60 min. (study 11) and 60 min. (study 13).

In study 2 (figs. 2 and 3) there was an average increase of 107 mg./100 ml. in the FBS, 31.8 Gm./24 hr. in the urinary glucose and 7 mg./100 ml. in the BUN associated with the administration of the 10 min. tryptic digest of BGH. These changes occurred within 2 days of the administration of the BGH preparation whereas, the increase in serum alkaline phosphatase of approximately 0.3 Bodansky units (B.U.)/100 ml. did not become apparent until the fifth day of injections. During the treatment period the patient went into negative nitrogen balance with an increase of 3.7 Gm./24 hr. in total urinary nitrogen and, subsequently, 178 mg./24 hr. in urinary creatine (table 3A). Urinary phosphorus, sodium and potassium were increased. The small increase in urinary calcium became evident on the fifth day of treatment and persisted during the post-treatment control period.

In study 11 (figs. 4 and 5) there was an average increase of 29 mg./100 ml. in the FBS and 2 mg./100 ml. in BUN, which occurred within 2 to 3 days of the administration of a 60 min. tryptic digest of BGH. There was no increase in urinary glucose, serum alkaline phosphatase or serum inorganic phosphorus (fig. 4). The total urinary nitrogen increased 1.2 Gm./24 hr. (fig. 5) with an associated increase in urinary creatine of 47 mg./24 hr. (table 3A) which returned to the pretreatment levels when treatment was discontinued. The urinary excretion of calcium, sodium and potassium were also increased (fig. 5).

In study 13 (figs. 6–9) there was little consistent change in the FBS or urinary glucose during the administration of a 60 min. tryptic digest of BGH

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Gastrointestinal Absorption of Recombinant Human Insulin-Like Growth Factor-I in Rats

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ABSTRACT

The GI absorption of recombinant human insulin-like growth factor-I (rhIGF-I) and its improvement were investigated in rats. The ^{125}I-rhIGF-I rapidly degraded to the trichloroacetic acid-soluble form in the small-intestinal contents, but it was relatively stable in the gastric and large-intestinal contents and in the subcellular fraction of the small-intestinal mucosa. To protect rhIGF-I from degradation in the small-intestinal contents, the effect of some adjuvants was examined and their degradation was markedly inhibited by the presence of aprotinin or casein. After p.o. administration of ^{125}I-rhIGF-I at the dose of 1.0 mg/kg, trichloroacetic acid-precipitable radioactivity in the plasma was periodically determined. We found that a considerable amount of rhIGF-I was absorbed into the systemic circulation and that the bioavailability was 9.3%, which is much greater than that of insulin. The coadministration of aprotinin and that of casein enhanced the bioavailability further: 46.9% and 67.0%, respectively. Radioimmunoassay using a monoclonal antibody for rhIGF-I confirmed the high bioavailability of immunoreactive rhIGF-I. From gel chromatography of plasma, the radioactivity in the plasma was found to be in the form of high-molecular-weight complexes. The mechanism for the uptake of rhIGF-I by intestinal mucosa may be absorptive-mediated endocytosis.

It has become possible to produce biologically active peptides and proteins that are therapeutically applicable by means of recombinant DNA technology. rhIGF-I, a peptide composed of 70 amino acids residues with a molecular weight of 7649, is one of them. IGF-I is an essential factor that controls the growth-promoting action. It has considerable homology with proinsulin but exerts its biological actions through specific IGF-I receptors (Humbel, 1990).

Recently, rhIGF-I has been used clinically to treat both Laron dwarfism, in which the function of the growth hormone receptor is deficient, and insulin-resistant diabetes. However, because frequent s.c. injections are needed for the therapy, the patients experience great discomfort. To improve the quality of life of such patients, an alternative method of administration is needed. We have already studied the nasal route as one substitute for s.c. injection and showed its utility as a novel route of administration of rhIGF-I in rats (Ukai *et al.*, 1996). However, p.o. administration is the most convenient route, and the development of its formulation for oral dosage would be of great value. Furthermore, IGF-I must be absorbed from the GI tract of the suckling newborn, because IGF-I in the maternal milk may play a role in regulating its postnatal development (Xu, 1996). Recently, Vacher *et al.* (1995) and Xu and Wang (1996) reported the absorption of IGF-I from the GI tract of neonatal calves and neonatal pigs, respectively. Furthermore, several protease inhibitors, including casein, are reported to be in the milk they ingest (Rao *et al.*, 1993). However, there is no information on the GI absorption of IGF-I in adult animals.

In the present study, to investigate the possibility of p.o. administration of rhIGF-I, we examined the GI absorption of rhIGF-I and its improvement in adult rats using several protease inhibitors.

Received for publication February 25, 1997.

Materials and Methods

Materials

The following drugs and chemicals were kindly provided by or obtained from the sources indicated: rhIGF-I, a monoclonal antibody (McAb) for rhIGF-I and ^{125}I-rhIGF-I (Fujisawa Pharmaceutical Co., Osaka, Japan), aprotinin (Teikokuzouki Pharmaceutical Co., Tokyo, Japan), casein (Nacalai Tesque Inc., Kyoto, Japan), DMβCD (Funakoshi Co., Tokyo, Japan), SGC, FD4 (average molecular weight 4400), colchicine, poly-L-lysine hydrobromide (molecular weight

ABBREVIATIONS: IGF-I, insulin-like growth factor-I; rhIGF-I, recombinant human insulin-like growth factor-I; McAb, monoclonal antibody; FD4, fluorescein isothiocyanate-dextran 4000; DMβCD, dimethyl β-cyclodextrin; SGC, sodium glycocholate; TCA, trichloroacetic acid; BBM, brush border membrane; BSA, bovine serum albumin; AUC, area under the plasma concentration *versus* time curve; MRT, mean residence time; C_{max}, maximum plasma concentration; T_{max}, time to reach C_{max}; RIA, radioimmunoassay; CL_{abs}, absorption clearance; IGFBP, IGF binding protein; DNP, 2,4-dinitrophenol.

Document 2. We have COPIED A GRAPH FROM A REPORT SHOWING AN INCREASE IN COW SERUM PROTEIN IN RBST MILK AS COMPARED TO CONTROL MILK(LEFT SIDE OF PAGE). AT THE LOWER RIGHT IS A CHART WHICH SHOWS THE INCREASED LEVEL OF COW SERUM PROTEIN ANTIBODIES IN DIABETIC CHILDREN.

Composition and Flavor of Milk Produced by Cows Injected with Recombinant Bovine Somatotropin[1]

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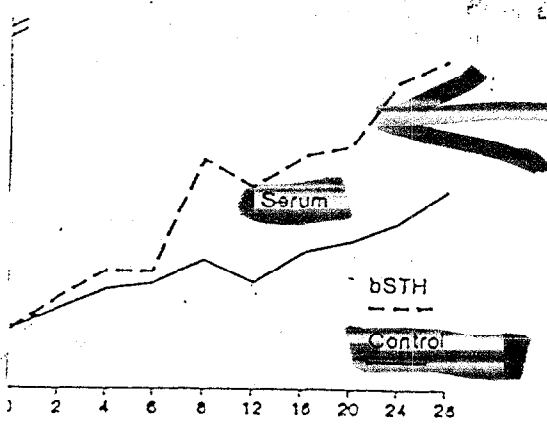

note

Milk protein content from control and cows on recombinant bovine somatotropin (bSTH) ment period.

Dairy Science Vol. 72, No. 6, 1989

Environmental Factors: Milk and Others

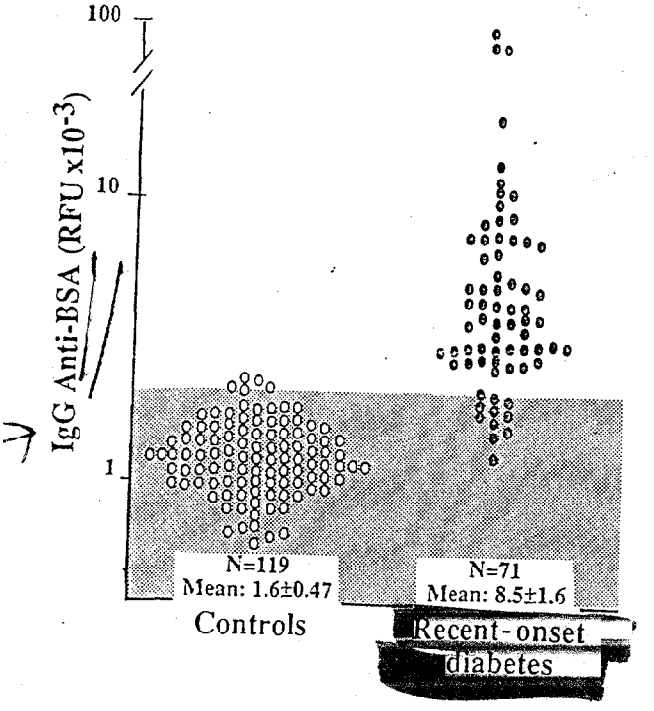

Figure 11.2. Anti-BSA antibody levels in a new series of Finnish children with recent-onset IDDM. Controls were age, sex and region matched. The shaded area includes 95% of all controls (mean±2SD), $p<0.0001$

Immunoglobulin antibovine serum antibody in children with diabetes. (from an article by Dosch et al. Diabetes: Prevention and Genetic Counseling in IDDM. Palmer editor.

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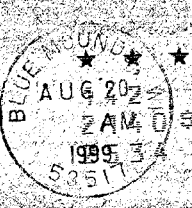

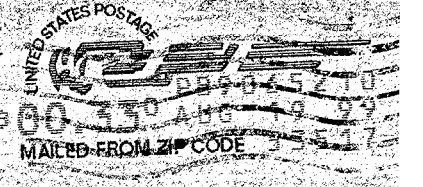

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